SUBJECT INDEX

A

Absorption
  dermal
    age-related changes in, 105–7, 117
  gastrointestinal
    age-related changes in, 106–7, 117
  pulmonary
    age-related changes in, 106–7, 117
Absorption enhancers, 459–61, 465
Acetazolamide, 238
Acetylcholine (ACh)
  cerebral blood flow and, 230–32, 234, 240–41
Acetylcholine binding site, 37–60
Acetylcholine-gated ion channel, 53–60
Acetylcholinesterase, 234, 507–9
  inhibition by soman of, 507–9
  organophosphate-mediated inhibition of, 507–9
N-acetyl-5-methoxytryptamine (See Melatonin)
N-acetylserotonin, 549–50
ACTH
  serotonin regulation of, 292–96, 309
Adenosine, 1–28, 242
  cerebral circulation and, 242
  renin release and, 1–28
Adenosine-brake hypothesis
  renin release and, 1–28
Adenosine 3'5'-monophosphate (Cyclic AMP), 550
Adenosine receptors, 1–28
  blockage of
    caffeine and, 14
Adenosine triphosphate
  cerebral circulation and, 242
Adenylate cyclase
  renin release and, 2–7, 27–28
Adiposity
  volume distribution of chemicals and, 107–8, 117
Affective disorders
  serotonin and, 289–309
Aflatoxin, 163
Agent Orange, 73
Aging (See Senescence)
Ah receptor, 73, 75–94, 179, 510
  dioxin binding and, 510
  dioxin-induced immunotoxicity and, 73, 75–94
  lymphocytes and, 83–94
Allosteric protein, 37–60
Aminophylline, 243
Angiotensin
  renin release and, 3–19, 22–25
Angiotensin II, 300
Antiarrythimic drugs, 427–49
  antifibrillatory vs., 442
  classification systems for, 430–35
  congestive heart failure and, 447–48
  guarded receptor theory of, 437–38
  mechanism of action of, 434–42
  modulated receptor theory of, 435–38
  proarrhythmia and, 442
Anticonvulsants
  fetal drug effects of, 528
Antifibrillatory drugs, 442
Anxiety
  cholecystokinin receptor antagonists and, 490–91
Anxiolytic drugs
  cholecystokinin antagonists and, 490–91
  CI-988 (PD135158), 491
Aquatic toxicology, 371–91
  chemical carcinogenesis and, 384–85
Arachidonate metabolites
  cytochrome P-450 and, 339–64
Arachidonic acid
  cytochrome P-450 and, 339–64
Arecoline, 240
Arrhythmia, 427–49
  calcium-blocking drugs for, 430, 441
  sodium-blocking drugs for, 427–49
Arylhydrocarbon hydroxylase, 79, 81–82
Asperlicin, 481
Asperlicin B, 481
Atrial natriuretic factor (ANF), 6–7

B

Bacteria
  cytochrome P-450 and, 177–98
Barbiturates, 177, 179, 184, 188, 191–96
Benzene retention
  increased adiposity and, 108
Benzodiazepine dependence
  cholecystokinin antagonist and, 491–92
Benzodiazepines, 104, 530
  enhanced sensitivity of elderly to, 104
BHT, 265
Bioconcentration factor, 374
Bladder carcinomas, 266–67
Blood vessels
  cerebrovascular circulation and, 229–45
Bradykinin, 129, 131–54
  cardiovascular system and, 142–45, 154
  gastrointestinal system and, 146–47
  inflammation and, 147–48, 154
  pain and, 147–48
  respiratory tract and, 148–50
  signal transduction and, 137
Bradykinin receptors, 129, 132–38, 150–53
  new receptor subtypes, 150–53
Brain-derived neurotrophic factor, 210
Bungarotoxin
  α-, 39, 42, 45
  neuronal, 39, 42
Busipirone, 294–95

C

Caffeine
  renin release and, 1, 11–12, 14–20
  renovascular hypertension and, 14–20
Calcium channel blockers, 243, 430, 441
  cerebral blood flow and, 243
Calcium/calmodulin-dependent protein kinase III, 212, 220
Cancer, 163–73, 321–35, 503–21
  liver, 163–73
  pharmocodynamics of, 503–21
  respiratory
    nickel-induced, 321–35
Carbachol, 240
Carbamazepine, 530

Carcinogenesis, 163–73, 253–81, 321–35, 384–85, 503–21
  chemical
    aquatic toxicology and, 384–85
    hormonal, 268–71
    mechanisms in, 253–81
    modulation of chronic energy intake restriction and, 171–73
  nickel-induced
    molecular mechanisms of, 321–35
  pharmacodynamic models of chemical, 503–21
  sustained tissue hyperplasia and, 253–81
Carcinogenesis studies
  chemical
    data for evaluation and policy setting from, 635–37
    experimental protocol and design, 628–31
    long-term, 621–49
    value and significance of, 621–49
Carcinogenicity
  levels of evidence of, 631–35
Carcinogens
  genotoxic, 254
  nongenotoxic, 254–81
    bladder carcinoma and, 266–67
    hepatocellular carcinoma and, 257
    intestinal cancer and, 275
    mouse skin tumors and, 271–72
    pathological and adaptive cellular changes and, 254–81
    renal cancer and, 272–73
    respiratory cancer and, 274
    subcutaneous sarcoma and, 255–57
    thyroid carcinoma and, 269–70
  nonmutagenic, 253–81
Carcinoma
  bladder, 266–67
  liver, 257–66
  renal, 272–73
  rodent forestomach, 267–68
  thyroid, 269–70
Cardiac Arrhythmic Pilot Study, 428, 447
Cardiac Arrhythmia Suppression Trial, 427–28
Catecholamine release, 212
Cell-mediated immunity
  dioxin exposure and, 74, 76–78, 83–85
Central nervous system disorders
  cholecystokinin receptors and, 469–70, 489–90
Cerebral blood flow, 229–45
  glucose utilization and, 236
  measurement methodologies of, 234–37
  protein synthesis and, 236
  tissue pH and, 236, 238
  undesirable drug effects on chronic obstructive pulmonary disease and, 243–44
    sleep apnea and, 243
    (See also Cerebrovascular circulation)
Cerebral resistance vessels, 233
Cerebrovascular circulation, 229–45
  acetylcholine synthesis and, 230–32, 234, 246–41
  enhancing, 239–43
  neurotransmitters and, 230–34, 239–43
  undesirable drug effects on, 243
    (See also Cerebral blood flow)
Cholecystokinin (CCK) receptor, 469–92
Cholecystokin receptor antagonists, 473–91
  gastrin-dependent disorders and, 488
  satiety and, 489
  spinal morphine analgesia and, 489
  treatment for biliary disorders and, 488
  treatment for pancreatis and, 488
  treatment of schizophrenia and, 489–90
Choline (Ch)
  cerebral blood flow and, 230–32, 240
Choline acetyl-transferase (Acetyl-CoA)
  cerebral blood flow and, 230–32
p-Chloroamphetamine, 291
Chloroform hepatocarcinogenicity, 512–14
p-Chlorophylaline (PCPA), 290
(^{3}H)Chlorpromazine, 53–54, 56
Chromosomes
  nickel-induced damage of, 330–35
CI-988 (PD134308), 484, 491
Cimetidine, 243
Circadian oscillators, 549–65
Circulation
  cerebrovascular, 229–45
  pharmacologic control of, 229–45
Cirrhosis of the liver
  hepatocellular carcinoma and, 257–59
Cocaine, 530
Computer simulation, 503–21
  pharmacodynamics and, 503–21
Computer technology
  pharmacokinetic modeling programs and, 464
Congenital adrenal hyperplasia, 539–40
Contaminants
  anthropogenic
    aquatic ecosystems and, 371–89
    chlorinated organic compounds, 373
    metals, 373
    polycyclic aromatic hydrocarbons, 373
  effects on aquatic organisms of, 380–89
  osmoregulation in fishes and, 380
Corticotropin releasing factor (CRF), 290, 292–96
Cysteine-191, 44, 47
Cysteine-193, 44, 47
Cytochrome P-450, 177–98, 260, 339–64, 377–78, 510
  arachidonic acid and, 339–64
  dioxin binding and, 510
  fish and, 377–78
  inducible bacterial, 177–98
    alcohol oxidation and, 186–87
    ether oxidation and, 186–87
    hydrocarbon oxidation and, 185–86
  induction of, 179–98
    barbiturate-mediated, 192–96
  inhibitors of metabolism of, 351
  liver enlargement and, 260
  nephron and, 343–48
  vascular, 348–56, 355–59
Cytochrome P-450d
  dioxin binding and, 510
Cytokines, 136
Cytolytic T-lymphocytes, 76–78

D

DDT, 167–68, 171, 265
Deletions
  nickel-induced, 332–35
Desipramine, 412
Devazepide, 471–72, 482, 487

2,7-Diclorodibenzo-*p*-dioxin (DCDD), 86–87
Dieldrin, 265
Di(2-ethylhexyl)phthalate (DEHP)
  liver enlargement and, 263–65
Diethylnitrosamine, 163, 167–71
Dihydro folate reductase, 506, 508
5,7-Dihyrdoxytryptamine (5,7-DHT), 291–94
Dioxin (See below; see 2,7-Dichlorodibenzo-*p*-dioxin; see 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin)
Dioxin-induced immunosuppression, 73–94
Dioxin-induced immunotoxicity
  Ah receptor and, 75–94
  calcium and, 89–91
  hormonal systems and, 91–94
  keratinocyte cell lines and, 80
  mechanisms of, 78–94
  phosphorylation and, 87–89
  thymic epithelial cells and, 80
Dioxin regulatory element, 75, 79
1,3-Dipropyl-8-(p-sulfophenyl)xanthine (DPSPX), 12–13
Disease
  pollution and, 371–91
Disposition, 101, 103
  altered
    age-related changes and, 103
Distribution
  age-related changes in 107–8, 117
Dizocilpine, 406–7, 412–13, 415–17
DNA damage
  nickel-induced, 328–35
Dopamine
  renin release and, 2, 4
Drug delivery
  ocular route of, 457–65
  pharmacokinetic modeling programs for, 464
Drug effects
  cerebrovascular circulation and, 229–45
    enhancing, 239–43
    impairing, 243
  fetotoxic, 525–43

E

Ecotoxicology, 371–91
Eicosanoids
  cerebral blood flow and, 242
Eicosatetrynoic acid (ETYA), 350
Endocrine tumor development, 268–71
β-Endorphin
  serotonin and, 296–97, 309
Endothelial-derived relaxing factor (EDRF), 6–7, 241
Enterochromaffin-like cells, 270–71
Environmental insults
  age-related changes in sensitivity to, 102–18
Epidermal growth factor, 134
Epinephrine, 239
Epoxyeicosatrienoic acids (EETs), 340–63
Estrogen, 91–92, 269–70
  dioxin-induced toxicity and, 91–92
  tumor development and, 269–70
Ethanol, 529, 537–38
Eukaryotes
  cytochrome P-450 and, 177, 196–98
Eutrophication, 372
Excitatory amino acids, 401–17
Excretion
  age-related changes in, 115–18
Exocytosis
  renin release and, 1–28
Eyedrops
  polypeptide, 457–65

F

Fenfluramine, 291
Fenofibrate, 263
Fetal drug effects, 525–43
  adverse, 526–38
  drug distribution and, 535–36
  drug metabolism and, 536
  organogenesis and, 528
Fetal injury
  death, 534
  functional retardation, 534
  growth retardation, 534
Fetal pharmacology, 525, 538–43
Fetal tachycardia, 540–42
Fetal toxoplasmosis, 538–39
Fetotoxic drugs, 525–43
Fish
  aquatic toxicology and, 371–91
  osmoregulation in
  effects of pollutants on, 380
  toxic chemicals in, 371–91
Flavin-containing monooxygenase (FMO), 378
Food coloring
  hepatocellular carcinoma and, 259
  subcutaneous sarcoma induction and, 256–57

G

G protein-coupled receptors
  high affinity (M-1) melatonin receptors and, 562–63
Gamma-amino butyric acid (GABA), 232
Gastrin
  tumor development and, 269–70
Gene sequences, 177
α_{2u}-Globulin
  renal cancer and, 273
Glucagon
  ocular delivery of, 458–63
  renin release and, 2,4
Glucuronidation
  age-related changes in, 112–13
Glutamate receptor, 401, 403, 412–13, 416
Glutamic-acid-decarboxylase (GAD), 232
Glutathione concentration
  age-related changes in, 113
Glycine site, 401, 403, 407–11
  NMDA receptor channel antagonist
Gonadotrophins
  tumor development and, 269
Growth factors, 205–22
GTPase activator protein, 219
Guarded receptor theory, 437–38
  sodium channel and

H

Halogenated aromatic hydrocarbons, 73–94
  immunocompetence and, 73–94
  structure-activity relationship studies of, 75
    (See also 2,7-Dichlorodibenzo-*p*-dioxin; 2,3,7,8-Tetrachlorodi-benzo-*p*-dioxin)
Halogenated hydrocarbon cytotoxicity, 511–14
  chloroform, 512–14
  1,1-dichloroethylene, 511
Hazard function
  carcinogenic effect and, 518–19

Hemodilution
  cerebrovascular circulation and, 239
Heparin, 530
Hepatocarcinogens, 163–73
  aflatoxin, 163
  aromatic amines, 163
  DDT, 167–68, 171
  diethylnitrosamine, 163, 167–71
  methyldiaminobenzidine, 170
  methylhydroxyethylnitrosamine, 170
  mycotoxins, 163
  nitrosamines, 163
  N-nitrosomorpholine, 170
  perfluorooctanoate, 167–68
  phenobarbital, 167, 169–71
  polychlorinated biphenyls, 170
  oxazepam, 167–68
  2,4,5-trichlorophenoxyacetic acid, 167–68
Hepatocarcinogenesis, 163–73
  kinetics of, 163–71
  modulation of, 164–73
    chronic energy intake restriction and, 171–73
    dietary, 171–73
    incidence and, 164–66
    infestation and, 171–72
    latency and, 164–66
    yield and, 164–66
α-Hexachlorocyclohexane, 265
Histrionicotoxin, 47
^{3}H-thymidine, 264, 273, 277
Humoral immune response
  dioxin exposure and, 75, 78–94
Hydroxyeicosatetraenoic acids, 341–64
5-Hydroxytryptamine (5-HT) (See Serotonin)
5-Hydroxytryptophan (5-HTP), 290
Hypercapnia, 242–43
Hyperemia, 353
Hyperplasia
  cancer and, 257–81
  sustained tissue, 257–81
Hypertension
  cytochrome P-450 and, 362–64
  kinins and, 142–45, 154
  renovascular, 1, 12–20
    caffeine and, 14–20
Hypertensive mechanisms, 339, 362–64

I

Ifenprodil, 407, 413–15
Imapramine, 412
Immediate-early response genes, 219–21
Immunocompetence, 73–94
  phosphorylation and, 88–89
Immunosuppression
  dioxin-induced, 73–94
Immunotoxicity
  dioxin-induced, 73–94
    Ah receptor and, 73, 75–94
    calcium and, 89–91
    hormonal systems and, 91–94
    keratinocyte cell lines and, 80
    mechanisms of, 78–94
    phosphorylation and, 87–89
    thymic epithelial cells and, 80
Incidence
  hepatocarcinogenesis and, 163–66
Indomethacin
  cerebral blood flow and, 242–43
  hypercapnia and, 242–43
Indoor air pollution
  radon exposure and, 569–93
Induction mechanisms, 177–98
  bacterial cytochrome P-450, 177–98
Inflammation
  kinins and, 132, 147–48, 154
Inositol triphosphate, 103–4
Insulin/glucagon
  ocular delivery of, 459–63
    permeation enhancers and, 459–61
Insulin-induced hyperglycemia
  serotonin and, 294–95
Interleukin-1, 134
Interleukin-2, 134, 209
Intrarenal baroreceptor system
  renin release and, 5, 9, 28
Invertebrates
  aquatic toxicology and, 371–91
2-(^{125}I)-Iodomelatonin binding, 554–55, 560–63
  affinity and density of, 561–62
Ionizing radiation
  radon progeny exposure, 569–93
Isapirone, 294–95, 299
Ischemia
  focal cerebral, 237
    cerebral vasodilators and, 237–39
Ischemic penumbra, 238–39, 243
Isotretinoin, 532

J

Juxtaglomerular cell, 1–10, 12, 16, 20–21, 27

K

Kallikrein, 129–31, 142
Kinetics, 163–73
  liver cancer, 163–73
  modulation of hepatocarcinogenesis and, 166–73
Kinin antagonists, 132, 138–53
Kinin receptors, 132–38, 150–53
  new subtypes of, 150–53
Kininogenase, 130
Kininogens, 130–31
Kinins, 129–54
  binding sites of, 129, 132–35
  hypertension and, 142–45, 154
  hypotensive shock and, 145–46
  pathophysiology of, 129, 130–34
    blood pressure and, 132
    circulatory homeostasis and, 132

L

Ligand-gated ion channel, 37–60
Lipopolysaccharide, 134
Lithium, 530
Liver cancer, 163–73 (See also Hepatocarcinogenesis, Hepatocarcinogens, Liver carcinoma)
Liver carcinoma, 257–66
  liver enlargement and, 265–66
  nongenotoxic carcinogens and, 257–66
  oral contraceptive use and, 278
Long-term potentiation (LTP)
  NMDA receptor and, 405
Long-term studies, 621–49
  data for evaluation and policy setting from, 635–37
  experimental protocol and design of, 628–31
  levels of evidence of carcinogenicity and, 631–35
Luteinizing hormone
  5-HT and, 308–9
Luzindole, 557–58
Lysylbradykinin, 131–32

M

Macula densa mechanism
renin release and, 5, 9, 21–23, 27–28
Mechanism of action
carcinogens and, 503–21
multiple, 517–18
teratogens and, 532–33
Melanogenesis
hair follicles and, 552
Melanophore pigment condensation, 550–53
Melanophores, 550–53
Melatonin, 549–65
chemical structure of, 531
inhibition of retinal dopamine release and, 553–58
Melatonin receptors, 549–65
cAMP and, 558–59
G protein-coupled, 559
G protein linkage of, 562–63
inhibition of cAMP formation and, 558
melanophore pigment condensation and, 550–53
ML-1, 563–64
pharmacology of, 552
Meproadifen, 47, 50
Metabolism
age-related changes in, 108–15, 117–18
glucuronidation and, 112–13
glutathione concentration and, 113
mixed function oxidase and, 109–11
sulfation and, 112–13
Metallothioneins, 382
Metabolism
transcellular, 339
Metals, 321–35, 374, 625
cancer and, 625
nickel-induced, 321–35
water quality and, 374
Methotrexate, 506, 508, 529
Methyldiaminobenzidine, 170
Methylhydroxyethylnitrosamine, 170
Microorganisms, 177–98
cytochrome P-450 and, 177–98
Mineralocorticoids, 340
Mixed function oxidase, 109–11
Mixed function oxidase enzymes, 259–63, 265
hepatocellular injury and, 259
ML-1 melatonin receptor, 563–64
Modulated receptor theory
sodium channel and, 435–38
Modulation
hepatocarcinogens and, 163–73
Monoamine oxidase inhibitors (MAOI), 290
Monooxygenases, 177–98, 339–64
herbicide-metabolizing, 181
hydrocarbon oxidations and, 185
P-450-dependent, 177–98, 339–64
Monro-Kellie Doctrine, 236
Muramyl depeptide, 134
Mutation
nickel-induced, 332–35

N

Nafenopin, 167
β-Naphthylamine, 266
National Organization for Rare Diseases, 604
Nephron, 339, 343–48, 361, 364
cytochrome P-450 system in, 343–48, 361, 364
Nerve growth factor (NGF), 205–22
cAMP and, 212–13
intracellular calcium concentration and, 212
PC12 cells and, 206–8
phospholipids and, 213
second messengers of, 211–13, 220–22
Nerve growth factor receptor, 207–11
Neuronal bungarotoxin, 39, 42, 45
Neuronal differentiation, 205–22
Neurotransmitters
cerebrovascular circulation and, 229–45
Nickel
bioavailability of, 323–28
carcinogenesis and, 321–35
chromatin damage and, 328–29
chromosome damage and, 330–34
DNA damage and, 328–35
Nicotinic aceylcholine receptor (AChR), 37–60
Nimodipine, 238–39
N-methyl-D-aspartate (NMDA) receptor channel, 401–17
anxiogenesis and, 402
blood pressure and, 402
developmental plasticity and, 402
epilepsy and, 402
glycine site of, 403, 407–11
hypoglycemia and, 402
ion-channel site of, 403, 404–7
learning and memory and, 402
olivopontocerebellar atropy and, 402
respiration and, 402
sensory transmission and, 402
transmitter recognition site of, 403–4
zinc site of, 411–13
N-Nitrosomorpholine, 170
Noncompetitive blockers
AChR ionic permeability and, 47–53
high-affinity site for, 47–53
low-affinity sites for, 48
Norepinephrine, 240
Norfenfluramine, 291

O

Ocular route
systemic drug delivery via, 457–65
Oppenheimer effect, 256
Organophosphates
inhibition of acetylcholinesterase by, 507–9
Orphan Drug Act, 604, 606–7, 609–10
Orphan drugs, 603–19
incentives to develop, 609, 612–13
laws regarding, 606–7, 609–10
Osmoregulation
water pollution and, 380
Oxazepam, 167–68
Oxytocin
serotonin and, 306–9

P

Pain
bradykinin and, 147–48
Pancreatitis
cholecystokinin antagonist and treatment of, 488
Papaverine, 238
PC12 cells
nerve growth factor and, 206–22
Perfluorooctanoate, 167–68
Pesticides, 623
Phagocytosis, 323–28
facultative, 323
nickel and, 323–35
Pharmacodynamic models, 503–21
biologically based, 503–21
empirical, 504–5

Pharmacodynamics
toxic chemicals and, 503–21
Pharmacokinetic model, 503–21
physiologically based, 505
Pharmacokinetics
age-related changes in, 104–18
Phencyclidine, 47, 405–7
Phenobarbital, 167, 169–71, 177, 179, 184, 188, 530
Phenobarbitone, 265
Phentolamine, 8
Phenylephrine, 239
Phenytoin, 529–31, 533
Phorbol esters, 134
Phosphatidylinositol, 341
Phosphatidylinositol turnover, 212
Phosphorylation
dioxin-induced immunotoxicity and, 87–90
Physostigmine
cerebral blood flow and, 238–41
Pilocarpine, 240
Pineal hormone, 549–65
Pollution
chemical, 371–91
disease and, 371–91
Polyamine site, 407, 414–15
Polychlorinated biphenyls, 170, 373–77
Puget Sound and, 373
Polypeptide eyedrops, 457–65
Polypeptides, 457–65
Polypharmacy
elderly and, 101
Ponceau MX, 259
Positron emission tomography (PET)
cerebral blood flow and, 237
Prednisolone
tyrosine aminotransferase induction and, 510
Premature ventricular depolarization, 428
Proarrythmia, 442–46
Prolactin, 92–94, 269, 279, 289, 297–300, 309
dioxin-induced toxicity and, 92–94
serotonin and, 297–300
tumor development and, 269, 279
Prolactin releasing factor (PRF), 297–300
Prolactin surge
estrogen-induced, 298
Prostacyclin, 242, 340
cerebral blood flow and, 242
Prostaglandin
cerebral blood flow and, 242
renin release and, 1, 5–6, 27–28
synthesis of nephron and, 344
Protein kinases
A, 213, 214, 216
C, 214, 216, 218, 220
N, 214
S6, 214
Protein methylation, 212
Protein phosphorylation, 214–18

R

Radon exposure
critical cells at risk from, 582–85
dosimetry models for, 577–93
epidemiology of, 585–86
research needs regarding, 590–93
risk assessment of, 573–93
smoking and, 588
raf-1, 215
Raphe nuclei, 290
Rare diseases and conditions
orphan drugs and, 603–19
ras gene, 205, 218–19
Registry of Tumors of Lower Animals, 385
Renal cancer, 272–73, 280
$\alpha_{2\mu}$-globulin and, 273
Renin, 300–4, 309
serotonin and, 300–4
sleep and, 303
stress and, 303
Renin release
adenosine and, 1–28
adenosine-brake hypothesis of, 1–28
adenylate cyclase model of, 2–7
caffeine and, 1, 11–12, 14–20
dopamine and, 2, 4
glucagon and, 2, 4
prostaglandins and, 1, 5–6, 27–28
Renin-releasing factor (RRF), 302–3
Retinoic acids, 529
Risk assessment, 503–21

S

Sarcoma
subcutaneous, 255–57
food coloring and, 256–57
induction of, 255
Schizophrenia
cholecystokinin antagonists and treatment for, 489–90
Scopolamine, 243
Senescence, 101–18, 321, 335
absorption and, 105–7, 117
α-adrenergic responsiveness and, 103
β-adrenergic responsiveness and, 103
dietary restriction and, 102
distribution and, 107–8, 117
environmental insults and, 102–17
excretion and, 115–17
metabolism and, 108–15, 117–18
steroids and 103
Serotonin (5-HT), 242, 289, 549–65
ACTH secretion and, 292–96
cerebral circulation and, 242
corticosterone secretion and, 292–96
β-endorphin secretion and, 296–97
insulin-induced hypoglycemia and, 294–95
luteinizing hormone and, 308–9
prolactin secretion and, 297–300
oxytocin and, 306–8
receptor subtypes, 292
renin secretion and, 300–4
vasopressin secretion and, 304–6
Shellfish
toxic chemicals in, 371–91
Signal transduction
bradykinin and, 137
Single photon emission computed tomography (SPECT), 238
Sodium channel blocking drugs
arrythmia and, 427–49
guarded receptor theory for, 437–38
modulated receptor theory for, 435–38
Spermidine, 414–15
Spermine, 414–15
Spiperone, 293–294
Sulfation
age-related changes in, 112–13
Systemic absorption
ocular route and, 457–65
permeation enhancers and, 459–61, 465
pharmocokinetics and, 464

T

Target organs, 644–46
T-cell replacing factor, 78

Teratogenesis
genetic influence on, 529–31
Teratology, 525–43
epidemiology of, 526–28
principles of, 528–43
2,3,7,8-Tetrachlorodibenzo-*p*-dioxin, 73–94, 105, 509–10
age-related changes in dermal absorption of, 105
Ah receptor and, 510
cellular targets for, 73–74
Ah receptor and, 73, 75
calcium and, 89–91
hormonal systems and, 91–94
cytochrome P-450d and, 510
immunosuppression and, 73–94
mechanisms of, 78–94
mechanism of action of pharmocokinetic model of, 509–10
Thalidomide
limb reductions and, 526–27, 529, 532
Theophylline
natriuresis and, 11–12, 22
Thromboxane, 340, 344
Thymic atrophy
dioxin-induced, 83–84
Thyroid dyshormonogenesis, 277
Thyroid-stimulating hormone (TSH), 269–70, 279
Thyrotropin-releasing hormone
ocular delivery of, 458–59
T-lymphocytes, 74, 76–78
cytolytic, 76
Torsades de pointes, 440–45
Toxic chemicals
pharmocodynamics of, 503–21
Toxicodynamics, 101, 103–18
Toxicokinetics, 101, 103–18
α-Toxins, 39–44
Toxoplasma gondii infection, 538
Transcellular metabolism, 339–64
Transmembrane negative feedback loop hypothesis, 2, 25–26
Transport modulation, 339–64
2,4,5-Trichlorophenocyacetic acid, 167–68
Triton X-100, 47
l-Tryptophan, 301
d-Tubocurarine, 42–43, 504–5
Tubuloglomerular feedback, 21
Tryptophan-149, 44
Tyrosine-93, 44–45
Tyrosine-190, 44–45
Tyrosine kinases, 205–209
T-lymphocyte antigens and, 209
Tyrosine phosphorylation, 215–18
NGF-induced, 216

U

Ultrasonography
transcranial doppler, 236–37

V

Valproic acid, 525–43
spina bifida and, 527–28, 531
Vasoactive intestinal polypeptide (VIP), 298, 300
Vasoconstriction
hypoxic pulmonary, 356
Vasodilation
cerebral blood flow and, 239–43
Vasopressin, 292, 304, 309
serotonin and, 304–6
Ventricular fibrillation, 446
Ventricular tachycardia, 428, 445
sustained, 445

W

Warfarin, 529
Water quality, 371–91

X

Xenobiotics, 101–18, 163–66, 180, 339, 371–91, 525–43
fetal pharmacology and, 525–43
waterborne
aquatic organisms and, 371–91

Y

Yield, 163–66

Z

Zinc site
NMDA receptor channel, 411–13